CURCUMIN SUPPRESSES METASTASIS IN A HUMAN BREAST CANCER XENOGRAFT MODEL: ASSOCIATION WITH SUPPRESSION OF NUCLEAR FACTOR-KAPPAB, CYCLOXYGENASE-2 AND MATRIX METALLOPROTEINASE

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Nontoxic and efficacious agents for the treatment of various malignant diseases including breast cancer are urgently needed. Curcumin (diferuloylmethane), a component of turmeric (*Curcuma longa*), is a potent chemopreventive agent that has been shown to downregulate the transcription factors NF-κB and AP-1; suppress expression of cyclin D1, MMP-9, COX2, iNOS, chemokines, HER2, and EGF receptor kinase; and inhibit angiogenesis. Currently, no effective treatment is available for metastatic breast cancer that follows surgery, radiation and chemotherapy for the primary tumor. We would like to exploit NF-κB for this because several genes involved in breast cancer metastasis are regulated by NF-κB. This transcription factor is activated in response to a variety of inflammatory stimuli, carcinogens, and chemotherapeutic agents. In the present report, we show that Taxol (paclitaxel) activated NF-κB through the activation of IκBα kinase and IκBα degradation in breast cancer cells leading to expression of COX2, cyclinD1 and MMP-9. We also show that curcumin inhibited Taxol-induced IKK activation, leading to suppression of NF-κB activation and expression of these NF-κB-dependent gene products. Curcumin also enhanced the Taxol-induced cytotoxicity of breast cancer cells. In a human breast cancer xenograft model, dietary administration to mice of curcumin and curcumin plus Taxol significantly decreased the incidence of breast cancer metastasis to the lung, and suppressed the expression of NF-κB, COX2, MMP-9 and Ki67. Overall, our results indicate that curcumin, which is a pharmacologically safe compound, has a useful therapeutic potential in preventing breast cancer metastasis in humans.

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